STN - Structure Search 12/3/07

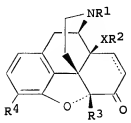
10/519,388

=> d ibib abs hitstr 1-3

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:41476 CAPLUS
DOCUMENT NUMBER: 140:111568
TITLE: Method for production of morphinan derivatives and the quaternary ammonium salts thereof substituted in position 14, and use thereof as highly-active analgesics or also as opioid antagonists
INVENTOR(S): Schmidhammer, Helmut; Spetea, Mariana; Schuetz, Johannes; Greiner, Elisabeth; Schuellner, Falko; Sailer, Bettina; Stuebegger, Kurt
PATENT ASSIGNEE(S): Austria
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005294	A2	20040115	WO 2003-EP6866	20030627
WO 2004005294	A3	20040513		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10229842	A1	20040205	DE 2002-10229842	20020703
CA 2491689	A1	20040115	CA 2003-2491689	20030627
AU 2003246627	A1	20040123	AU 2003-246627	20030627
EP 1554282	A2	20050720	EP 2003-762539	20030627
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1665819	A	20050907	CN 2003-815881	20030627
JP 2006500326	T	20060105	JP 2004-518608	20030627
IN 2004CN03045	A	20060217	IN 2004-CN3045	20041231
US 2005182258	A1	20050818	US 2005-519388	20050317
PRIORITY APPLN. INFO.:			DE 2002-10229842 A	20020703
			WO 2003-EP6866 W	20030627

OTHER SOURCE(S): MARPAT 140:111568
GI



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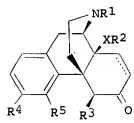
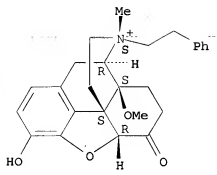


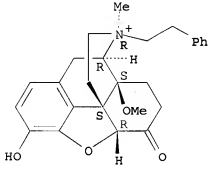
II



● I⁻

RN 646033-65-0 CAPLUS
CN Morphinanium, 4,5-epoxy-3-hydroxy-14-methoxy-17-methyl-6-oxo-17-(2-phenylethyl)-, iodide, (5α,17R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● I⁻

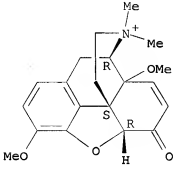
L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:406154 CAPLUS
DOCUMENT NUMBER: 75:6154
ORIGINAL REFERENCE NO.: 75:1027a,1030a
TITLE: Methanolysis of 14-bromocodeinone dimethyl acetal
AUTHOR(S): Heinisch, G.; Klintz, V.; Vieboeck, Franz
CORPORATE SOURCE: Pharm.-Chem. Inst., Univ. Wien, Vienna, Austria
SOURCE: Monatsh. Chem. (1971), 102(2), 530-7
CODEN: MOCHAP
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The products of methanolysis in the presence of Na2CO3 were 25% 7-methoxyneopinone dimethyl acetal (I), isolated as its methyl perchlorate, and 23% 14-methoxycodeinone dimethyl acetal. On heating dilute NaOH I underwent Hofmann degradation to 7-methoxyneopinone dimethyl acetal methine methyl perchlorate.
IT 32392-03-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 32392-03-3 CAPLUS
CN 14ξ-Morphinanium, 7,8-didehydro-4,5α-epoxy-3,14-dimethoxy-17,17-dimethyl-6-oxo-, perchlorate (8CI) (CA INDEX NAME)

CM 1

CRN 47385-08-0
CMF C20 H24 N O4

Absolute stereochemistry.



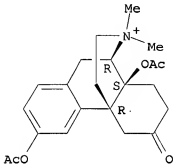
CM 2

CRN 14797-73-0
CMF Cl O4

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1969:11856 CAPLUS
DOCUMENT NUMBER: 70:11856
ORIGINAL REFERENCE NO.: 70:2231a,2234a
TITLE: Elimination of the 4-hydroxyl group of the alkaloids related to morphine. XI. Synthesis of (-)-14-hydroxy-3-methoxy-N-methylmorphinan derivatives
AUTHOR(S): Sawa, Y. K.; Tada, H.
CORPORATE SOURCE: Shionogi Res. Lab., Shionogi and Co., Ltd., Osaka, Japan
SOURCE: Tetrahedron (1968), 24(20), 6185-96
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 70:11856
AB Ullmann reaction of 14-hydroxydihydrothebainone followed by Na-liquid NH3 reduction gave (-)-14-hydroxy-3-methoxy-6-oxo-N-methylmorphinan in high yield. Starting from this compound 6-Me derivs. were synthesized.
IT 21020-40-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 21020-40-6 CAPLUS
CN Morphinanium, 3,14-dihydroxy-17,17-dimethyl-6-oxo-, iodide, diacetate

(8CI) (CA INDEX NAME)

Absolute stereochemistry.



● I-

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=> d his

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L1             STRUCTURE UPLOADED
L2               2 S L1
L3              36 S L1 FULL

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L4               3 S L3

=> d l1
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L1             STR
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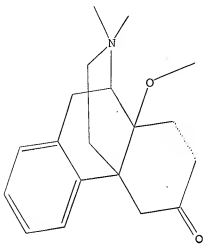

Structure attributes must be viewed using STN Express query preparation.

10/519,388

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STN- Structure Search 12/3/07

10/519,388

=> d ibib abs hitstr 1-40

L4 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN

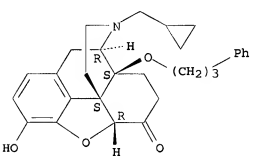
ACCESSION NUMBER: 2007:894767 CAPLUS
DOCUMENT NUMBER: 147:433134
TITLE: OSAR study on the antinociceptive activity of some morphinans
AUTHOR(S): Ramirez-Galicia, Guillermo; Garduno-Juarez, Ramon; Hemmateenejad, Bahram; Deeb, Omar; Deciga-Campos, Myrna; Moctezuma-Eugenio, Juan Carlos
CORPORATE SOURCE: Instituto de Ciencias Fisicas, Universidad Nacional Autonoma de Mexico, Cuernavaca, 62250, Mex.
SOURCE: Chemical Biology & Drug Design (2007), 70(1), 53-64
CODEN: CBDDAL; ISSN: 1747-0277
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Quant. structure-activity relationship studies were performed to describe and predict the antinociceptive activity of 31 morphinan derivs. reported by the US Drug Evaluation Committee in 2005 and 2006. From these, three data sets were constructed and several models were calculated following the multiple linear regression and Leave-One-Out Cross-Validation (LOO-CV) tests. In general, these models achieved good descriptive power (approx. 92%) as well as predictive power (approx. 76%), but were unable to predict an external validation set of morphinan derivs. When artificial neural networks were applied to these models, an improvement of the predictive and external validation values was obtained. It was observed that the results of the NN models are significantly better that those obtained by multiple linear regression. In spite that the problem under investigation can be handled adequately by a linear model, a neural network does bring slight improvements in the predictive power.

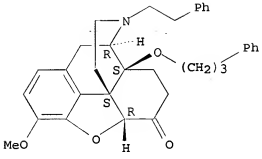
IT 547767-39-5 609844-14-6 609844-19-1
609844-22-6 609844-26-0 646032-55-5
646033-24-1 646033-25-2 646033-33-2
646033-37-6 646033-44-5 646033-47-8
646033-48-9 646033-51-4 646033-52-5
646033-68-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(OSAR study on the antinociceptive activity of some morphinans)

RN 547767-39-5 CAPLUS
CN Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3-hydroxy-14-(3-phenylpropoxy)-, (5α)- (CA INDEX NAME)

Absolute stereochemistry.

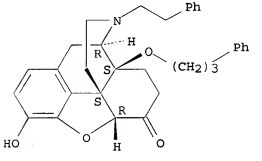


RN 609844-14-6 CAPLUS
CN Morphinan-6-one, 4,5-epoxy-3-methoxy-5,17-dimethyl-14-(3-phenylpropoxy)-, (5α)- (CA INDEX NAME)



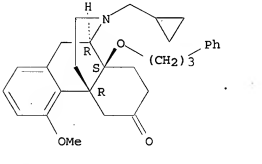
RN 646033-52-5 CAPLUS
CN Morphinan-6-one, 4,5-epoxy-3-hydroxy-17-(2-phenylethyl)-14-(3-phenylpropoxy)-, (5α)- (CA INDEX NAME)

Absolute stereochemistry.



RN 646033-68-3 CAPLUS
CN Morphinan-6-one, 17-(cyclopropylmethyl)-4-methoxy-14-(3-phenylpropoxy)-(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:632772 CAPLUS
DOCUMENT NUMBER: 145:83563
TITLE: Preparation of opioid conjugates containing a nitrooxy moiety for use in pharmaceutical compositions for treating pain
INVENTOR(S): Smith, Maree Therese
PATENT ASSIGNEE(S): The University of Queensland, Australia

SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006066362	A1	20060629	WO 2005-AU1976	20051223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005318883	A1	20060629	AU 2005-318883	20051223
CA 2592407	A1	20060629	CA 2005-2592407	20051223
EP 1838714	A1	20071003	EP 2005-821596	20051223
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRIORITY APPLN. INFO.:			AU 2004-907352	A 20041224
			WO 2005-AU1976	W 20051223

OTHER SOURCE(S): MARPAT 145:83563
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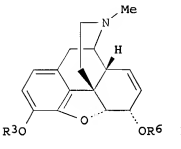

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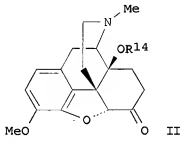


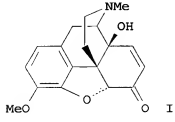
II

AB Opioid conjugates, such as Q-[OCO(CH2)nONO2]m [Q = opioid moiety; m = number of esterified hydroxyl groups on opioid moiety, i.e. 1, 2, etc.; n = 1, 4, etc.], were prepared for therapeutic use as analgesics acting as slow-release nitric oxide donors. Thus, morphine conjugate I (R3 = H, R6 = COCH2ONO2) was prepared via an esterification reaction in 59% yield of ClCOCH2ONO2 with morphine I (R3 = R6 = H) using dicyclohexylcarbodiimide in anhydrous CHCl3. Opioid conjugates I [R3 = H, R6 = CO(CH2)4ONO2; R3 = R6 = CO(CH2)4ONO2] and II [R14 = CO(CH2)4ONO2] were similarly prepared from morphine or oxycodone. The prepared opioid conjugates were assayed for antinociceptive activity in rats.

IT 894357-74-5P 894357-76-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrooxy opioid conjugates for therapeutic use as analgesics

L4 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:470410 CAPLUS
DOCUMENT NUMBER: 143:153551
TITLE: Mechanistic Diversity of the van Leusen Reaction Applied to 6-Ketomorphinans and Synthetic Potential of the Resulting Acrylonitrile Substructures
AUTHOR(S): Schuetz, Johannes; Windisch, Petra; Kristeva, Elka; Wurst, Klaus; Ongania, Karl-Hans; Horvath, Ulrike E. I.; Schottenberger, Herwig; Laus, Gerhard; Schmidhammer, Helmut
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Institute of Pharmacy and Center for Molecular Biosciences Innsbruck, University of Innsbruck, Innsbruck, 6020, Austria
SOURCE: Journal of Organic Chemistry (2005), 70(13), 5323-5326
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:153551
GI



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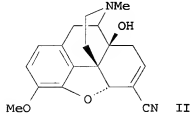

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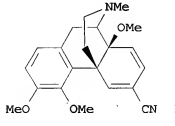
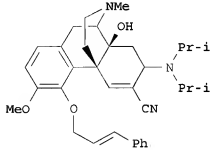


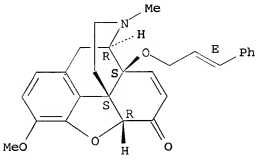
III



IV

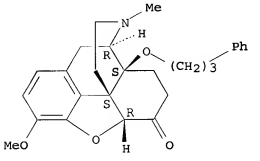
AB Tosylmethyl isocyanide was used to convert 7,8-didehydro-6-ketomorphinans, e.g. I, to 6,7-didehydromorphinan-6-carbonitriles, e.g. II, with retainment of the 4,5-epoxy ring. However, ring opening occurred in the presence of NaH giving 5,6,7,8-tetradehydromorphinan-6-carbonitriles, e.g. III. Addition of nucleophiles such as Li diisopropylamide or Grignard reagents to the acrylonitrile substructure yielded ring-opened 5,6-didehydro products, e.g. IV. Seven products were characterized by X-ray crystal structure anal. and revealed insight into the mechanistic diversity of the van Leusen reaction.
IT 528854-52-6 528854-53-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(van Leusen reaction/reductive cyanation of 6-ketomorphinans and Grignard and nucleophilic addition reactions of resulting acrylonitriles)
RN 528854-52-6 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[[(2E)-3-phenyl-2-propenyl]oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 528854-53-7 CAPLUS
CN Morphinan-6-one, 4,5-epoxy-3-methoxy-17-methyl-14-(3-phenylpropoxy)-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

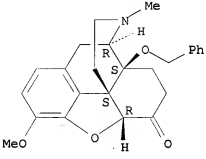


REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:307054 CAPLUS
DOCUMENT NUMBER: 143:19240
TITLE: Synthesis and Biological Evaluation of 14-Alkoxymorphinans. 22. Influence of the 14-Alkoxy Group and the Substitution in Position 5 in 14-Alkoxymorphinan-6-ones on in Vitro and in Vivo Activities
AUTHOR(S): Lattanzi, Roberta; Spetea, Mariana; Schuellner, Falko; Rief, Silvia B.; Krassnig, Roland; Negri, Lucia; Schmidhammer, Helmut
CORPORATE SOURCE: Department of Human Physiology and Pharmacology, University 'La Sapienza', Rome, I-00185, Italy
SOURCE: Journal of Medicinal Chemistry (2005), 48(9), 3372-3378
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:19240
AB Novel 14-alkoxy-substituted (e.g. allyloxy, benzyloxy, naphthylmethoxy) morphinan-6-one derivs. were synthesized and biol. evaluated. Compds. 6-9 and 11 displayed affinities in the subnanomolar range to μ opioid receptors which were comparable to 14-O-methyloxymorphone (1) and

CN Morphinan-6-one, 4,5-epoxy-3-methoxy-17-methyl-14-(phenylmethoxy)-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

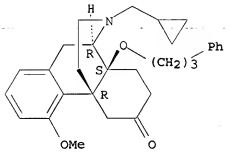


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN

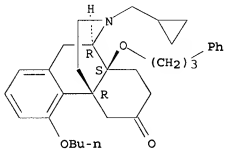
ACCESSION NUMBER: 2005:127600 CAPLUS
DOCUMENT NUMBER: 142:348119
TITLE: 3D-QSAR Comparative Molecular Field Analysis on Opioid Receptor Antagonists: Pooling Data from Different Studies
AUTHOR(S): Peng, Youyi; Keenan, Susan M.; Zhang, Qiang; Kholodovych, Vladyslav; Welsh, William J.
CORPORATE SOURCE: Department of Pharmacology and the Informatics Institute of UMDNJ, University of Medicine Dentistry of New Jersey-Robert Wood Johnson Medical School (UMDNJ-RWJMS), Piscataway, NJ, 08854, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(5), 1620-1629
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three-dimensional quant. structure-activity relationship (3D-QSAR) models were constructed using comparative mol. field anal. (Co-MFA) on a series of opioid receptor antagonists. To obtain statistically significant and robust Co-MFA models, a sizable data set of naltrindole and naltrexone analogs was assembled by pooling biol. and structural data from independent studies. A process of "leave one data set out", similar to the traditional "leave one out" cross-validation procedure employed in partial least squares (PLS) anal., was utilized to study the feasibility of pooling data in the present case. These studies indicate that our approach yields statistically significant and highly predictive Co-MFA models from the pooled data set of δ, μ, and κ opioid receptor antagonists. All models showed excellent internal predictability and self-consistency: q2 = 0.69/r2 = 0.91 (δ), q2 = 0.67/r2 = 0.92 (μ), and q2 = 0.60/r2 = 0.96 (κ). The Co-MFA models were further validated using two sep. test sets: one test set was selected randomly from the pooled data set, while the other test set was retrieved from other published sources. The overall excellent agreement between Co-MFA-predicted and exptl. binding affinities for a structurally diverse array of ligands across all three opioid receptor subtypes gives testimony to the superb predictive power of these models. Co-MFA field anal. demonstrated that the variations in binding affinity of opioid antagonists are dominated by steric rather than electrostatic interactions with the three opioid receptor binding sites. The Co-MFA steric-electrostatic contour maps corresponding to the δ, μ, and κ opioid



RN 646033-69-4 CAPLUS
CN Morphinan-6-one, 4-butoxy-17-(cyclopropylmethyl)-14-(3-phenylpropoxy)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:802693 CAPLUS
DOCUMENT NUMBER: 141:301467
TITLE: Compounds and methods for lowering the abuse potential and extending the duration of action of a drug, such as an opioid analgesic
INVENTOR(S): Shafer, Jules A.; Telyatnikov, Vladislav V.; Guo, Zhiwei
PATENT ASSIGNEE(S): Controlled Chemicals, Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004082620	A2	20040930	WO 2004-US7910	20040315
WO 2004082620	A3	20050915		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2518834	A1	20040930	CA 2004-2518834		20040315
US 2004204434	A1	20041014	US 2004-800898		20040315
US 7230005	B2	20070612			
EP 1603597	A2	20051214	EP 2004-757462		20040315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK					
JP 2006520392	T	20060907	JP 2006-507215		20040315
EP 1782834	A2	20070509	EP 2007-3844		20040315
EP 1782834	A3	20070801			
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR					
US 2007203165	A1	20070830	US 2007-742566		20070430

PRIORITY APPLN. INFO.:

US 2003-454253P	P	20030313
EP 2004-757462	A3	20040315
US 2004-800898	A3	20040315
WO 2004-US7910	W	20040315

AB The abuse potential of a bioavailable drug, such as an opiate analgesic agent, is reduced and its duration of action is extended by converting it to a poorly absorbed ester prodrug or other prodrug derivative prior to formulation. Unlike many existing sustained release formulations of active pharmaceutical agents wherein an active pharmaceutical agent can be released by chewing, crushing, or otherwise breaking tablets or capsule beads containing the active pharmaceutical agent, such mech. processing of tablets or capsule beads containing a prodrug of this invention neither releases the active drug nor compromises the controlled conversion of prodrug to drug. Moreover, tablets and capsule beads containing prodrugs of this invention or other drugs can be formulated with a sufficient amount of a thickening agent such as hydroxypropyl Me cellulose or CM-cellulose to impede inappropriate i.v. and nasal administration of formulations that are not indicated for these modes of administration. For example, an oxycodone ester prodrug, 2-(benzyloxycarbonylamino)pentanedioic acid 1-(3-methoxy-14-hydroxy-6,7-didehydro-[4,5]α-epoxy-17-methylmorphinan-6-yl) ester was prepared The prodrug had a lower binding affinity for the μ opioid receptor than the analgesic drug oxycodone.

IT 765304-97-0P

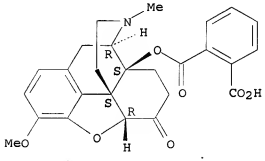
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of prodrugs of opioid analgesic for lowering abuse potential and extending duration of action)

RN 765304-97-0 CAPLUS

CN Morphinan-6-one, 14-[(2-carboxybenzoyl)oxy]-4,5-epoxy-3-methoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:377144 CAPLUS
DOCUMENT NUMBER: 141:89262

TITLE: Synthesis and Biological Evaluation of 14-Alkoxymorphinans. 21. Novel 4-Alkoxy and 14-Phenylpropoxy Derivatives of the μ Opioid Receptor Antagonist Cyprodime

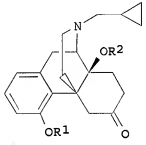
AUTHOR(S): Spetea, Mariana; Schuellner, Falko; Moisa, Radu C.; Berzetei-Gurske, Ilona P.; Schraml, Barbara; Doerfler, Cynthia; Aceto, Mario D.; Harris, Louis S.; Coop, Andrew; Schmidhammer, Helmut

CORPORATE SOURCE: Department of Pharmaceutical Chemistry Institute of Pharmacy, University of Innsbruck, Innsbruck, A-6020, Austria

SOURCE: Journal of Medicinal Chemistry (2004), 47(12), 3242-3247
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:89262

GI



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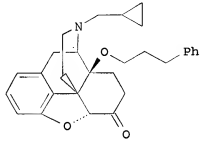
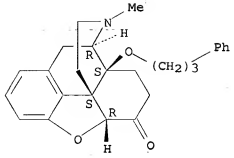


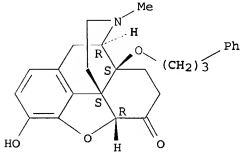
III

AB The synthesis, biol., and pharmacol. evaluation of novel derivs. of cyprodime are described. Their binding affinities at μ, δ, and κ opioid receptors were evaluated using receptor binding assay. It was observed that the affinity of these compds. was sensitive to the character and length of the substituent in position 4. Further prolongation of the 4-alkoxy group of cyprodime (I; R1, R2 = Me) and its 4-butoxy analog I (R1 = n-C4H9, R2 = Me) is detrimental for the μ opioid receptor affinity. Introduction of an arylalkoxy group at C-4 does not increase μ affinity in the case of benzyloxy, while a phenylpropoxy group reduces μ affinity. The δ and κ affinities were also reduced compared to the reference compds. A significant increase in the affinity at the μ opioid receptors was achieved by introducing a 14-phenylpropoxy group. Increases in the affinity at δ and κ receptors were also observed. These findings provide further evidence that the nature of the substituent at position 14 has a major impact on the abilities of morphinans to interact with opioid receptors. In the [35S]GTPγS binding assay, all tested compds. were partial agonists at μ and δ receptors. Compds. I [R1 = Me, R2 = (CH2)3Ph (II)] and III showed antagonism at κ receptors, while compound I [R1 = H, R2 = (CH2)3Ph (IV)] exhibited some partial agonist activity at this receptor. The novel derivs. of cyprodime containing a 14-phenylpropoxy group acted as potent antinociceptives. When tested in vivo, compds. IV, II, and III were considerably more potent than morphine, with phenol IV showing the highest antinociceptive potency (21-fold in the hot plate test, 38-fold in the tail flick test, and 300-fold in the paraphenylquinone writhing test) in mice. Introduction of a 14-phenylpropoxy substituent leads to a



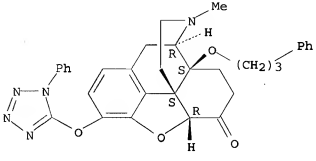
RN 646033-04-7 CAPLUS
CN Morphinan-6-one, 4,5-epoxy-3-hydroxy-17-methyl-14-(3-phenylpropoxy)-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 646033-22-9 CAPLUS
CN Morphinan-6-one, 4,5-epoxy-17-methyl-14-(3-phenylpropoxy)-3-[(1-phenyl-1H-tetrazol-5-yl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:213436 CAPLUS
DOCUMENT NUMBER: 140:386044
TITLE: Medicinal agent for treatment of opioid addiction
INVENTOR(S): Romanov, I. V.
PATENT ASSIGNEE(S): Russia
SOURCE: Russ., No pp. given
CODEN: RUXXE7

DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RU 2221566	C1	20040120	RU 2003-104582	20030217

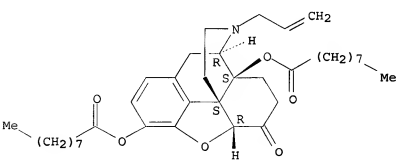
PRIORITY APPLN. INFO.: RU 2003-104582 20030217
OTHER SOURCE(S): MARPAT 140:286044

AB The invention relates to an agent used for treatment of opiomania. The medicinal agent consists of antagonists of opiate receptors and a pharmaceutically acceptable carrier. As antagonists of opiate receptors, esters of N-substituted 14-hydroxymorphinans are used; as a carrier natural oils, esters of carboxylic acid with 8-16 carbon atoms and low-mol. alcs. are used, sulfolanes, propylene carbonate, N,N-dimethylacetamide or their mixture are used taken in the definite ratio of components. The invention provides the development of highly effective low toxic an antirelapse agent with prolonged opioprotective effect being after a single s.c. or i.m. injection.

IT 267221-13-6P 663618-05-1P 667455-23-4P
685869-49-2P 685869-50-5P 685869-53-8P
685869-54-9P 685869-55-0P 686337-67-7P
686337-69-9P 686337-71-3P 686337-73-5P
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(medicinal agent for treatment of opioid addiction)

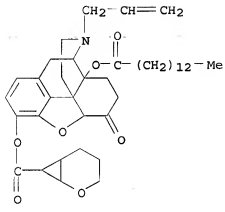
RN 267221-13-6 CAPLUS
CN Morphinan-6-one, 4,5-epoxy-3,14-bis[(1-oxononyl)oxy]-17-(2-propenyl)-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



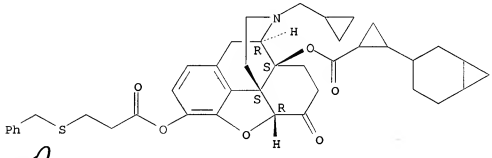
RN 663618-05-1 CAPLUS
CN Morphinan-6-one, 4,5-epoxy-3-[(1-oxotetradecyl)oxy]-17-(2-propenyl)-14-[(spiro[2.4]hept-1-ylcarbonyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 686337-73-5 CAPLUS
CN Morphinan-6-one, 14-[[[2-(bicyclo[4.1.0]hept-3-yl)cyclopropyl]carbonyl]oxy]-17-(cyclopropylmethyl)-4,5-epoxy-3-[1-oxo-3-[(phenylmethyl)thio]-1-oxopropoxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Inventor

L4 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:41476 CAPLUS
DOCUMENT NUMBER: 140:111568
TITLE: Method for production of morphinan derivatives and the quaternary ammonium salts thereof substituted in position 14, and use thereof as highly-active analgesics or also as opioid antagonists
INVENTOR(S): Schmidhammer, Helmut; Spetea, Mariana; Schuetz, Johannes; Greiner, Elisabeth; Schuellner, Falko; Sailer, Bettina; Stuebegger, Kurt
PATENT ASSIGNEE(S): Austria
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005294	A2	20040115	WO 2003-EP6866	20030627
WO 2004005294	A3	20040513		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

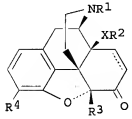
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10229842	A1	20040205	DE 2002-10229842		20020703
CA 2491689	A1	20040115	CA 2003-2491689		20030627
AU 2003246627	A1	20040123	AU 2003-246627		20030627
EP 1554282	A2	20050720	EP 2003-762539		20030627
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1665819	A	20050907	CN 2003-815881		20030627
JP 2006500326	T	20060105	JP 2004-518608		20030627
IN 2004CN03045	A	20060217	IN 2004-CN3045		20041231
US 2005182258	A1	20050818	US 2005-519388		20050317
PRIORITY APPLN. INFO.:			DE 2002-10229842	A	20020703
			WO 2003-EP6866	W	20030627

OTHER SOURCE(S): MARPAT 140:111568

GI



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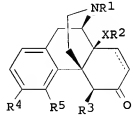
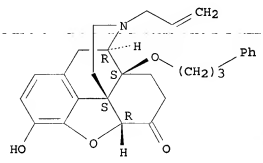


II

AB The invention relates to a class of morphinan compds. I [R1 = C1-6-alkyl, C2-6-alkenyl, C2-6-alkynyl, C3-16-cycloalkyl, C7-16-arylalkyl, C8-16-arylalkenyl, C8-16-arylalkynyl; R2 = H, C4-6-alkyl, C2-6-alkenyl, C2-6-alkynyl, C3-16-cycloalkyl, C7-16-arylalkyl, C8-16-arylalkenyl, C8-16-arylalkynyl, C2-6-alkenoyl, C2-6-alkynoyl, C9-16-arylalkenoyl, C9-16-arylalkynoyl; R3 = C1-6-alkyl, C2-6-alkenyl, C7-16-arylalkyl, C8-16-arylalkenyl, C1-6-alkoxy-(C1-6-alkyl); R4 = H, OH, C1-6-alkoxy, C2-10-alkoxyalkoxy, C2-6-alkenyloxy, C2-6-alkynyloxy, C3-13-cycloalkoxy, C4-16-cycloalkenyloxy, C4-16-cycloalkynyloxy, C7-16-arylalkoxy, C8-16-arylalkenyloxy, C8-16-arylalkynyloxy, C1-6-alkanoyloxy, C3-6-alkenoyloxy, C3-6-alkynoyloxy, C7-16-arylalkanoyloxy, C9-16-arylalkenoyloxy, C9-16-arylalkynoyloxy; X = O, S, CH2; dashed line = single or double bond] and II [R5 = H, OH, C1-6-alkoxy, C2-10-alkoxyalkoxy, C2-6-alkenyloxy, C2-6-alkynyloxy, C3-13-cycloalkoxy, C4-16-cycloalkenyloxy, C4-16-cycloalkynyloxy, C7-16-arylalkanoyloxy, C8-16-arylalkenoyloxy, C8-16-arylalkynoyloxy, C2-6-alkanoyloxy] and the quaternary ammonium salts thereof, substituted in position 14, which may be used as highly-active analgesics or also as opioid antagonists. Thus, morphinan I [R1 = cyclopropylmethyl, R2 = (CH2)3Ph, R3 = H, R4 = OH, X = O, dashed line = single bond] was prepared from 10β-hydroxycodeinone (I; R1 = Me, R2 = R3 = H, R4 = OMe, X = O, dashed line = double bond), via O-alkylation with cinnamyl bromide, hydrogenation of both double bonds, N-demethylation, N-alkylation with (bromomethyl)cyclopropane and O-demethylation. The invention further relates to the pharmaceutically-acceptable salts and easily-produced derivs. thereof, a process for production thereof and use thereof in the production of pharmaceutical

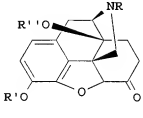


● HCl

L4 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:936892 CAPLUS
DOCUMENT NUMBER: 140:235925
TITLE: Method for preparing N-substituted 14-hydroxymorphinane esters of carboxylic acids
INVENTOR(S): Romanov, I. V.; Fedorov, I. S.; Linskii, I. V.; Ukrainets, I. V.
PATENT ASSIGNEE(S): Otkrytoe Aktsionernoe Obshchestvo "Mezhdunarodnaya Nauchno-Tekhnologicheskaya Korporatsiya", Russia
SOURCE: Russ., No pp. given
CODEN: RUXXE7
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RU 2215741	C1	20031110	RU 2002-129376	20021105

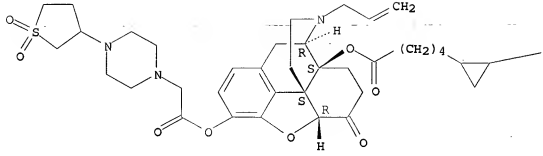
PRIORITY APPLN. INFO.: RU 2002-129376 20021105
OTHER SOURCE(S): CASREACT 140:235925; MARPAT 140:235925
GI



I

AB Invention relates to N-substituted 14-hydroxymorphinane esters that are important narcotic analgetics and/or antagonistic agents antagonists of opiate receptors of prolonged effect and to methods for their preparing Invention describes N-substituted 14- hydroxymorphinane esters I [R = allyl, cyclopropylmethyl, R' = C19-25-aliphatic carboxylic acids, unsatd. C19-25-carboxylic acids (with a single double bond), polyunsatd. C10-15-carboxylic acids (with 2-3 double bonds), unsatd. C10-15-carboxylic

PAGE 1-A



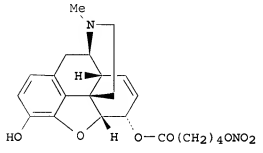
PAGE 1-B

L4 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:757712 CAPLUS
DOCUMENT NUMBER: 139:271069
TITLE: Methods and compositions including nitric oxide donors and opioid analgesics for pain relief
INVENTOR(S): Smith, Maree Therese; Brown, Lindsay; Harvey, Mark Bradford Pullar; Williams, Craig Mckenzie
PATENT ASSIGNEE(S): The University of Queensland, Australia
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078437	A1	20030925	WO 2003-AU335	20030320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2479098	A1	20030925	CA 2003-2479098	20030320
AU 2003209850	A1	20030929	AU 2003-209850	20030320
US 2003219494	A1	20031127	US 2003-393050	20030320
EP 1495026	A1	20050112	EP 2003-744274	20030320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
JP 2005524676	T	20050818	JP 2003-576442	20030320
CN 1703416	A	20051130	CN 2003-809229	20030320
IN 2004DN02856	A	20070302	IN 2004-DN2856	20040923
PRIORITY APPLN. INFO.:			US 2002-366594P	P 20020320

WO 2003-AU335 W 20030320
WO 2003-AU353 W 20030320

OTHER SOURCE(S): MARPAT 139:271069
GI



I

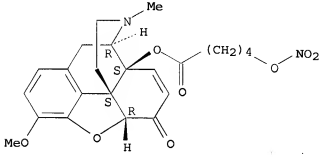
AB Compns. and methods that induce, promote or otherwise facilitate pain relief are disclosed. These compns. and methods comprise a nitric oxide donor which either directly or indirectly prevents, attenuates or reverses the development of reduced opioid sensitivity, together with a compound which activates the opioid receptor that is the subject of the reduced opioid sensitivity. The compns. and methods prevent or alleviate pain, especially in neuropathic conditions and even more especially in peripheral neuropathic conditions such as painful diabetic neuropathy. The preferred nitric oxide donor is L-arginine, while the preferred compds. which activate the opioid receptor are morphine and oxycodone. Conjugate compds. comprising the nitric oxide donor and an opioid analgesic are also disclosed. Preparation of morphine-NO donor conjugates, e.g. I, is also described.

IT 602298-14-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitric oxide donors and opioid analgesics for pain relief)

RN 602298-14-6 CAPLUS

CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[[5-(nitrooxy)-1-oxopentyl]oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:678621 CAPLUS
DOCUMENT NUMBER: 139:219311
TITLE: Tamper-resistant transdermal opioid delivery devices
INVENTOR(S): Shevchuk, Ihor; Cassidy, James P.; Reidenberg, Bruce;

Sharp, Dale E.; Kupper, Robert J.
PATENT ASSIGNEE(S): Euro-Celtique, S.A., Luxembourg
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070191	A2	20030828	WO 2003-US4999	20030219
WO 2003070191	A8	20040610		
WO 2003070191	A3	20040910		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004033253	A1	20040219	US 2003-366394	20030214
AU 2003216321	A1	20030909	AU 2003-216321	20030219
EP 1476141	A2	20041117	EP 2003-742830	20030219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006502967	T	20060126	JP 2003-569151	20030219

PRIORITY APPLN. INFO.:
US 2002-357139P P 20020219
US 2002-357141P P 20020219
WO 2003-US4999 W 20030219

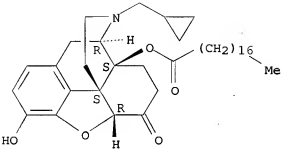
AB This invention relates to a tamper-resistant transdermal-delivery device comprising an opioid, or its salt, and an acyl opioid antagonist, or a salt. The transdermal-delivery device allows an analgesically effective amount of the opioid, or a salt, to be transdermally administered to a patient. The invention further relates to methods for treating or preventing pain in a patient comprising contacting the skin of a patient with the transdermal-delivery device of the invention for an amount of time sufficient to treat or prevent pain. Thus, 3-(p-anisoylnaltrexone) (I) was prepared by the reaction of naltrexone-HCl with p-anisoyl chloride in 10% naHCO3 solution The base was converted to its HCl salt. Thus, an aqueous gel contained EtOH 221., hydroxyethyl cellulose 1.9, anhydrous fentanyl 1.0, I 20.0, and water to 100% by weight This gel was loaded onto a reservoir-type transdermal delivery polymeric device.

IT 111129-16-9 586364-74-1 586364-76-3
586364-86-5 586364-88-7 586365-08-4
586365-10-8 586365-20-0 586365-22-2
586365-32-4 586365-33-5 586365-42-6
586365-54-0 586365-56-2 586365-93-7
586365-95-9 586366-04-3 586366-06-5
586366-29-2 586366-31-6 586366-42-9
586366-44-1 586366-55-4 586366-57-6
586366-68-9 586366-70-3 586366-80-5
586366-82-7 586367-07-9 586367-08-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tamper-resistant transdermal opioid delivery devices)

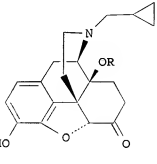
RN 111129-16-9 CAPLUS

CN Morphinan-6-one, 14-(3-carboxy-1-oxopropoxy)-17-(cyclopropylmethyl)-4,5-epoxy-3-hydroxy-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



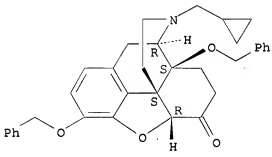
L4 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:661396 CAPLUS
DOCUMENT NUMBER: 140:27951
TITLE: Effect of 14-O-benzylation on the opioid receptor affinity and antagonist potency of naltrexone
AUTHOR(S): Schuellner, Falko; Meditz, Ruth; Krassnig, Roland; Morandell, Guenther; Kalinin, Valery N.; Sandler, Ellen; Spetea, Mariana; White, Angela; Schmidhammer, Helmut; Berzetei-Gurske, Ilona P.
CORPORATE SOURCE: Division of Pharmaceutical Chemistry, Department of Pharmacy, University of Innsbruck, Innsbruck, A-6020, Austria
SOURCE: Helvetica Chimica Acta (2003), 86(7), 2335-2341
CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:27951
GI



I

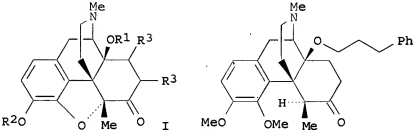
AB The 14-O-benzylnaltrexones I (R = PhCH2, 2-MeC6H4, 2-ClC6H4, 3-ClC6H4) were prepared from naltrexone in several steps. The novel compds. were biol. evaluated in radioligand binding and in [35S]GTPγS functional assays in comparison to the reference compound naltrexone. In the binding assay, compds. I exhibited preference for κ opioid receptors, while the parent compound naltrexone shows preference for μ receptors. In the functional assay, μ antagonist potency of compds. I was in the range of naltrexone, while κ antagonist potency was considerably higher for most novel compds. in comparison to naltrexone.

IT 633303-32-9P 633303-33-0P 633303-34-1P
633303-35-2P 633303-40-9P 633303-41-0P
633303-42-1P 633303-43-2P



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:623187 CAPLUS
DOCUMENT NUMBER: 139:292382
TITLE: Synthesis and Biological Evaluation of 14-Alkoxymorphinans. 20. 14-Phenylpropoxymetopon: An Extremely Powerful Analgesic
AUTHOR(S): Schuetz, Johannes; Spetea, Mariana; Koch, Martin; Aceto, Mario D.; Harris, Louis S.; Coop, Andrew; Schmidhammer, Helmut
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Institute of Pharmacy, University of Innsbruck, Innsbruck, A-6020, Austria
SOURCE: Journal of Medicinal Chemistry (2003), 46(19), 4182-4187
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:292382
GI



AB The synthesis and the biol. and pharmacol. evaluation of several 14-phenylpropoxy analogs of 14-methoxymetopon, I (R1 = 3-phenylpropyl, R2 = Me, H, prop-2-ynyl, R3 = H) and II are described. Thus, reacting I (R1 = H, R2 = Me, R32 = bond) with NaH/DMF and cinnamyl bromide gave I (R1 = 3-phenylpropyl, R3 = H) in 45% yield. Most of the new compds. were nonselective and exhibited binding affinities in the subnanomolar or low nanomolar range at opioid receptors (μ, κ, δ), with 14-phenylpropoxymetopon (PPOM) I (R1 = 3-phenylpropyl, R2 = R3 = H) (III) displaying the highest affinity for all three opioid receptor types. The most striking finding of this study is that the derivs. from the novel series of N-methyl-14-phenylpropoxymorphinans acted as extremely powerful antinociceptives with potencies higher than that of 14-methoxymetopon and even etorphine. 14-Phenylpropoxymetopon (PPOM) III showed considerably

L4 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:491234 CAPLUS
DOCUMENT NUMBER: 139:53193
TITLE: Method for the production of 6-aminomorphinan derivatives and their use as highly active analgesics
INVENTOR(S): Schuetz, Johannes; Schmidhammer, Helmut
PATENT ASSIGNEE(S): Austria
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051888	A1	20030626	WO 2002-EP14343	20021216
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10161963	A1	20030703	DE 2001-10161963	20011217
CA 2470809	A1	20030626	CA 2002-2470809	20021216
AU 2002356660	A1	20030630	AU 2002-356660	20021216
EP 1456212	A1	20040915	EP 2002-804904	20021216
EP 1456212	B1	20061206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002015027	A	20041109	BR 2002-15027	20021216
CN 1604900	A	20050406	CN 2002-825128	20021216
HU 2005000024	A2	20050428	HU 2005-24	20021216
JP 2005516937	T	20050609	JP 2003-552770	20021216
NZ 533966	A	20060526	NZ 2002-533966	20021216
AT 347555	T	20061215	AT 2002-804904	20021216
ES 2278083	T3	20070801	ES 2002-2804904	20021216
RU 2306314	C2	20070920	RU 2004-121952	20021216
ZA 2004004752	A	20050211	ZA 2004-4752	20040615
IN 2004CN01539	A	20060210	IN 2004-CN1539	20040709
NO 2004003016	A	20040715	NO 2004-3016	20040715
US 2005038061	A1	20050217	US 2004-499133	20040921
PRIORITY APPLN. INFO.:			DE 2001-10161963 A	20011217
			WO 2002-EP14343 W	20021216

OTHER SOURCE(S): MARPAT 139:53193
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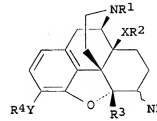
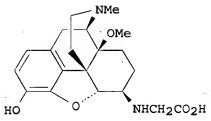


I



II

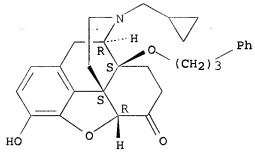
AB The invention relates to the compds., e.g., I [R1 = H, C1-6-alkyl, C2-6-alkenyl, C2-6-alkynyl, C1-6-monohydroxyalkyl, C1-6-dihydroxyalkyl, C1-6-trihydroxyalkyl, C3-10-cycloalkyl-C1-6-alkyl, C3-10-cycloalkyl-C2-6-alkenyl, C3-10-cycloalkyl-C2-6-alkynyl, C6-10-aryl-C1-6-alkyl, C6-10-aryl-C2-6-alkenyl, C6-10-aryl-C2-6-alkynyl; R2 = R1, C2-6-alkanoyl, C3-6-alkenoyl, C3-6-alkynoyl, C6-10-aryl-C1-6-alkyl, C6-10-aryl-C3-6-alkenoyl, C6-10-aryl-C3-6-alkynoyl; R3 = H, C1-6-alkyl, C2-6-alkenyl, C6-10-aryl-C1-6-alkyl, C6-10-aryl-C1-6-alkyl, C6-10-aryl-C2-6-alkenyl, C1-6-alkoxy, -C1-6-alkyl, CO2(C1-6-alkyl), CO2H, CH2OH; R4 = C1-6-alkyl, C2-6-alkenyl, C2-6-alkynyl, C3-10-cycloalkyl-C1-6-alkyl, C3-10-cycloalkyl-C2-6-alkenyl, C3-10-cycloalkyl-C2-6-alkynyl, C6-10-aryl-C1-6-alkyl, C6-10-aryl-C2-6-alkenyl, C6-10-aryl-C2-6-alkynyl, etc.; R5, R6 = H C3-10-cycloalkyl-C1-6-alkyl, C3-10-cycloalkyl-C2-6-alkenyl, C3-10-cycloalkyl-C2-6-alkynyl, C6-10-aryl-C1-6-alkyl, C6-10-aryl-C2-6-alkenyl, C6-10-aryl-C2-6-alkynyl, etc.; X = O, S, CH2; XR2 = H; Y = O; YR4 = H], and their pharmaceutically acceptable acid addition salts, which are useful as highly active analgesics. Thus, aminomorphinan II·1.5 CF3CO2H was prepared from 14-O-methoxymorphone hydrobromide via reductive amination with glycine tert-Bu ester in MeOH containing NaCNBH3 followed by deesterification with CF3CO2H in CH2Cl2. Aminomorphinan II·1.5 CF3CO2H was tested for analgesic activity [Ki = 0.83 nM for opioid receptor; ED50 = 28 μg/kg s.c. and ED50 = 0.42 μg/kg i.cv. in rat tail flick test; ED50 = 500 μg/kg s.c. and ED50 = 0.42 μg/kg i.cv. respiratory depression in rats; ED50 = 100 μg/kg s.c. antiallodynic effect in rats].

IT 547767-39-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, analgesic activity and reductive amination of, with amino acids; preparation of 6-aminomorphinane derivs. for use as highly active analgesics)

RN 547767-39-5 CAPLUS

CN Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3-hydroxy-14-(3-phenylpropoxy)-, (5α)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:242768 CAPLUS

DOCUMENT NUMBER: 138:401935

TITLE: Synthesis and Biological Evaluation of 14-Alkoxymorphinans. 18.N-Substituted 14-Phenylpropyloxymorphinan-6-ones with Unanticipated Agonist Properties: Extending the Scope of Common Structure-Activity Relationships

AUTHOR(S): Greiner, Elisabeth; Spetea, Mariana; Krassnig, Roland; Schuellner, Falko; Aceto, Mario; Harris, Louis S.; Traynor, John R.; Woods, James H.; Coop, Andrew; Schmidhammer, Helmut

CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Institute of Pharmacy, University of Innsbruck, Innsbruck, A-6020, Austria

SOURCE: Journal of Medicinal Chemistry (2003), 46(9), 1758-1763
CODEN: JMCMAR; ISSN: 0022-2623

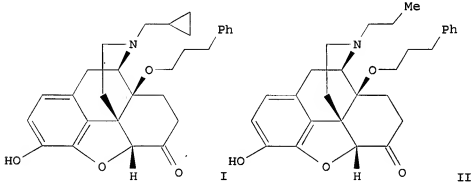
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

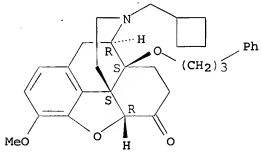
OTHER SOURCE(S): CASREACT 138:401935

GI



AB The synthesis, biol., and pharmacol. evaluations of 14β-O-phenylpropyl-substituted morphinan-6-ones are described. The most striking finding of this study was that all of the compds. from the novel series of differently N-substituted 14β-O-phenylpropylmorphinans acted as powerful opioid agonists. Even with N-substituents such as

Absolute stereochemistry.

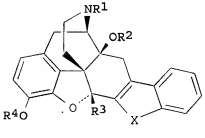


● HCl

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:827072 CAPLUS
DOCUMENT NUMBER: 138:56114
TITLE: Synthesis and Biological Evaluation of 14-Alkoxymorphinans. 17. Highly δ Opioid Receptor Selective 14-Alkoxy-Substituted Indolo- and Benzofuromorphinans
AUTHOR(S): Schuetz, Johannes; Dersch, Christina M.; Horel, Robert; Spetea, Mariana; Koch, Martin; Meditz, Ruth; Greiner, Elisabeth; Rothman, Richard B.; Schmidhammer, Helmut
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Institute of Pharmacy, University of Innsbruck, Innsbruck, A-6020, Austria
SOURCE: Journal of Medicinal Chemistry (2002), 45(24), 5378-5383
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:56114
GI

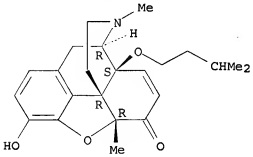


I

AB 14-Alkoxy analogs of naltrindole and naltriben differently substituted in positions 5 and 17 and at the indole nitrogen [compds. I (R1 = CPM, R2 =

benzofuromorphinans as δ opioid receptor antagonists)
RN 478285-41-5 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-hydroxy-5,17-dimethyl-14-(3-methylbutoxy)-, hydrobromide, (5α)- (9CI) (CA INDEX NAME)

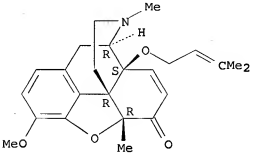
Absolute stereochemistry.



● HBr

IT 478285-32-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of; preparation and biol. evaluation of 14-alkoxy-substituted indolo- and benzofuromorphinans as δ opioid receptor antagonists)
RN 478285-32-4 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-5,17-dimethyl-14-[(3-methyl-2-butenyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:177388 CAPLUS
DOCUMENT NUMBER: 134:340585
TITLE: Photochemical N-demethylation of alkaloids
AUTHOR(S): Ripper, J. A.; Tiekink, E. R. T.; Scammells, P. J.
CORPORATE SOURCE: School of Biological and Chemical Sciences, Deakin University, Geelong, 3217, Australia
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(4), 443-445
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:340585

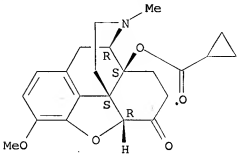
AB Certain alkaloids were observed to undergo N-demethylation processes under photochem. conditions. Tropine, acetyltropine, tropinone, and atropine were cleanly N-demethylated upon treatment with tetraphenylporphin, oxygen, and light. Dextromethorphan also underwent a N-demethylation reaction, but reacted further to afford an imine. In contrast, 14-acyloxycodeinones underwent a photochem. induced tandem N-demethylation-acyl migration.

IT 70866-71-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(photochem. N-demethylation of alkaloids)

RN 70866-71-6 CAPLUS

CN Morphinan-6-one, 14-[(cyclopropylcarbonyl)oxy]-4,5-epoxy-3-methoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

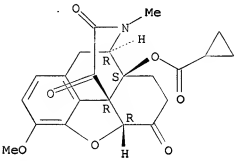


IT 338743-03-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(photochem. N-demethylation of alkaloids)

RN 338743-03-6 CAPLUS

CN Morphinan-6,15,16-trione, 14-[(cyclopropylcarbonyl)oxy]-4,5-epoxy-3-methoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

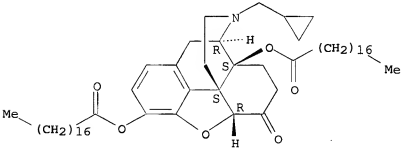


REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:52039 CAPLUS
DOCUMENT NUMBER: 134:266461
TITLE: Synthesis of naltrexone distearate
AUTHOR(S): Feng, Li-Hua; Jing, Ling; Wu, Chun-Ying; Hu, Ming-Yang; Yang, Min

CORPORATE SOURCE: Jiangsu Institute of Nuclear Medicine, Wuxi, 214063, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2000), 31(10), 437-438
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Title compound was synthesized from naltrexone hydrochloride via esterification with stearic acid at 3- and 14- position.
IT 331865-43-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of naltrexone distearate)
RN 331865-43-1 CAPLUS
CN Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3,14-bis[(1-oxooctadecyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

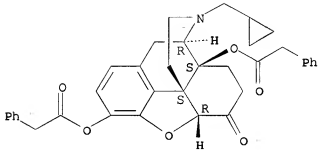
Absolute stereochemistry.



L4 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:355531 CAPLUS
DOCUMENT NUMBER: 132:322019
TITLE: Preparation of naloxone and naltrexone ester derivatives
INVENTOR(S): Lu, Zhengtang
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

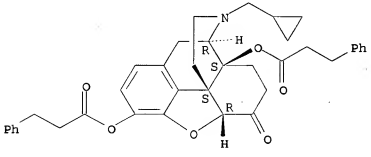
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1204649	A	19990113	CN 1997-112842	19970704
CN 1050130	B	20000308		
PRIORITY APPLN. INFO.:			CN 1997-112842	19970704

OTHER SOURCE(S): MARPAT 132:322019
GI



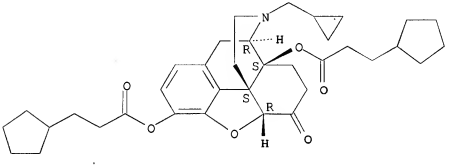
RN 267221-30-7 CAPLUS
CN Morphinan-6-one, 17-(cyclopropylmethyl)-4,5-epoxy-3,14-bis(1-oxo-3-phenylpropoxy)-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 267221-31-8 CAPLUS
CN Morphinan-6-one, 3,14-bis(3-cyclopentyl-1-oxopropoxy)-17-(cyclopropylmethyl)-4,5-epoxy-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:33058 CAPLUS
DOCUMENT NUMBER: 130:182631
TITLE: Synthesis and biological evaluation of 14-alkoxymorphinans. 16. 14-O-Alkyl derivatives of the μ opioid receptor antagonist cyprodime
AUTHOR(S): Schmidhammer, Helmut; Krassnig, Roland; Greiner, Elisabeth; Traynor, John R.
CORPORATE SOURCE: Institute of Pharmaceutical Chemistry, University of Innsbruck, Innsbruck, A- 6020, Austria

SOURCE: Heterocycles (1998), 49, 489-498
CODEN: HTCYAM; ISSN: 0385-5414
PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:182631

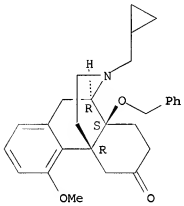
AB The 14-O-benzyl derivs. of cyprodime and 3-hydroxycyprodime were synthesized in several steps from 3-desoxynaltrexone and naltrexone, resp. In the mouse vas deferens preparation it was found that a 14-O-benzyl group could enhance μ opioid receptor affinity in cyprodime while the μ affinity of 3-hydroxycyprodime was not changed.

IT 220556-48-9P 220556-49-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. evaluation of 14-O-benzyl derivs. of cyprodime)

RN 220556-48-9 CAPLUS

CN Morphinan-6-one, 17-(cyclopropylmethyl)-4-methoxy-14-(phenylmethoxy)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

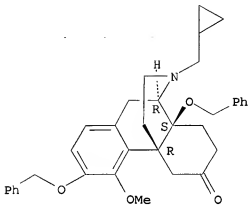


● HCl

RN 220556-49-0 CAPLUS

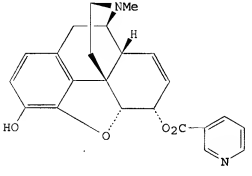
CN Morphinan-6-one, 17-(cyclopropylmethyl)-3-hydroxy-4-methoxy-14-(phenylmethoxy)-, hydrobromide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:218248 CAPLUS
DOCUMENT NUMBER: 120:218248
TITLE: Synthesis and analgetic activity of nicotinic esters of morphine derivatives
AUTHOR(S): Hosztafi, S.; Kohegyi, I.; Simon, C.; Furst, Z.
CORPORATE SOURCE: Alkaloida Chem. Co. Ltd., Tiszavasvari, Hung.
SOURCE: Arzneimittel-Forschung (1993), 43(11), 1200-3
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



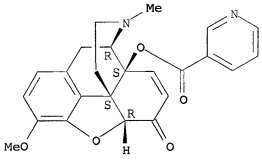
AB The synthesis of morphine nicotinates, e.g. I, is described using nicotinyl chloride in the presence of pyridine. Isomorphine and isocodeine nicotinates were prepared from the corresponding morphine and codeine derivs. with nicotinic acid in the presence of triphenylphosphine and di-Et azodicarboxylate. Unexpectedly the reaction of 14-hydroxydihydromorphinone derivs. was anomalous; enol esters were formed. The analgetic activity of selected compds. was determined

IT 104134-14-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as analgesic)

RN 104134-14-7 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(3-

pyridinylcarbonyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

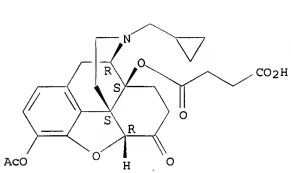


L4 ANSWER 23 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:605099 CAPLUS
DOCUMENT NUMBER: 107:205099
TITLE: Coupling of naltrexone to biodegradable poly(α-amino acids)
AUTHOR(S): Negishi, Naoki; Bennett, David B.; Cho, Chong Su; Jeong, Seo Young; Van Heeswijk, Wolfgang A. R.; Feijen, Jan; Kim, Sung Wan
CORPORATE SOURCE: Dep. Pharm., Univ. Utah, Salt Lake City, UT, 84112, USA
SOURCE: Pharmaceutical Research (1987), 4(4), 305-10
CODEN: PHREEB; ISSN: 0724-8741
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The narcotic antagonist naltrexone (I) was modified at the 3 and 14 OH positions and covalently coupled to a biodegradable poly(α-amino acid) backbone through a labile bond. Selective acetylation of I with acetic anhydride gave I 3-acetate (II), which was subsequently succinoylated to I 3-acetate-14-hemisuccinate (III) with succinic anhydride. The polymeric backbone chosen for initial coupling expts. was poly-N5-(3-hydroxypropyl)-L-glutamine (PHPG). The side-chain OH functionality permitted covalent bonding of III through an ester linkage. Hydrolysis of covalently bound drug to give I or its derivs. (II and III) should be much slower than diffusion of drug through the polymer matrix. While hydrolysis of I from the polymer side chain is first order, the release of drug from the matrix can be zero order due to the geometry of the device and the phys. and chemical interactions between I and the polymer matrix. iN vitro studies of PHPG-I conjugate in disk form did not show constant release because of the hydrophilic nature of the polymer backbone and the changing local chemical environment upon hydrolysis of drug-polymer linkages. The conjugated system was made more hydrophobic by coupling drug to copolymers of hydroxypropyl-L-glutamine (HPG) and L-leucine. Conjugates of III coupled with copoly(HPG-70/Leu-30) demonstrated a nearly constant, but slightly declining release rate of I and its derivs. for 28 days in vitro.

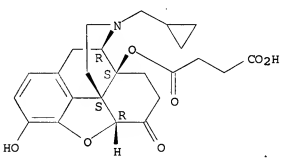
IT 111129-15-8P, Naltrexone-3-acetate-14-hemisuccinate
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and coupling to poly(amino acids))
RN 111129-15-8 CAPLUS
CN Morphinan-6-one, 3-(acetyloxy)-14-(3-carboxy-1-oxopropoxy)-17-(cyclopropylmethyl)-4,5-epoxy-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 111129-16-9, Naltrexone-14-hemisuccinate
RL: PROC (Process)
(release of, from naltrexone-poly(amino acid) conjugates)
RN 111129-16-9 CAPLUS
CN Morphinan-6-one, 14-(3-carboxy-1-oxopropoxy)-17-(cyclopropylmethyl)-4,5-epoxy-3-hydroxy-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:22671 CAPLUS
DOCUMENT NUMBER: 92:22671
ORIGINAL REFERENCE NO.: 92:3861a,3864a
TITLE: N-Alkyl-14-hydroxymorphinans and derivatives
INVENTOR(S): Olofson, Roy A.; Pepe, Joseph P.
PATENT ASSIGNEE(S): Research Corp., USA
SOURCE: U.S., 16 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

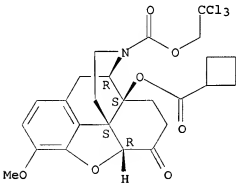
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4161597	A	19790717	US 1976-751571	19761220
PRIORITY APPLN. INFO.:			US 1976-751571 A	19761220

OTHER SOURCE(S): MARPAT 92:22671
GI For diagram(s), see printed CA Issue.
AB The hydroxymorphinans I CR = C1-5 alkyl, Ph, C1-5 alkanoyl, C3-6 cycloalkylcarbonyl, (un)substituted phenylalkanoyl; R1 = R2 = H, R1 R2 = O; R3 = C1-5 alkyl, C3-6 cycloalkyl, (un)substituted phenylalkyl; (X = O, H2) were prepared Thus, 14-(cyclobutylcarbonyl)noroxycodone-HCl was treated with NaHCO3 to give N-(cyclobutylcarbonyl)noroxycodone, which was

converted to the ethylene ketal followed by reduction, hydrolysis, and demethylation to give N-(cyclobutylmethyl)noroxymorphone.

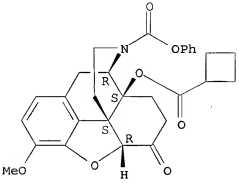
IT 70866-68-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(ketalization of)
RN 70866-68-1 CAPLUS
CN Morphinan-17-carboxylic acid, 14-[(cyclobutylcarbonyl)oxy]-4,5-epoxy-3-methoxy-6-oxo-, 2,2,2-trichloroethyl ester, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 72186-15-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with sodium hydroxide)
RN 72186-15-3 CAPLUS
CN Morphinan-17-carboxylic acid, 14-[(cyclobutylcarbonyl)oxy]-4,5-epoxy-3-methoxy-6-oxo-, phenyl ester, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

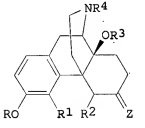


L4 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:457263 CAPLUS
DOCUMENT NUMBER: 91:57263
ORIGINAL REFERENCE NO.: 91:9291a,9294a
TITLE: N-Dealkylation of N-alkyl-14-hydroxymorphinans and derivatives
INVENTOR(S): Olofson, Roy A.; Pepe, Joseph P.
PATENT ASSIGNEE(S): Research Corp., USA
SOURCE: U.S., 14 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 4141897	A	19790227	US 1976-751570		19761220
PRIORITY APPLN. INFO.:			US 1976-751570	A	19761220

OTHER SOURCE(S): MARPAT 91:57263
GI



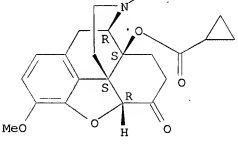
AB N-Alkylhydroxymorphinans I [R = C1-6 alkanoyl, phenylalkanoyl, C3-6 cycloalkylcarbonyl, C1-5 alkyl, C3-5 cycloalkyl, cycloalkylalkyl, phenylalkyl, alkyl- and alkoxyphenylalkyl; R1R2 = O, R1 = R2 = H; R3 = C1-6 alkanoyl, C3-6 cycloalkylcarbonyl, Bz, substituted Bz, phenylalkanoyl, alkyl- and alkoxyphenylalkanoyl; R4 = C1-6 alkyl, phenylalkyl, C3-6 cycloalkyl, cycloalkylalkyl; Z = O, H2] underwent N-dealkylation by acylation to give I [R4 = H2C:CHO2C, XH2CH2O2C, X2HCCH2O2C, X3CCH2O2C (X = halo)] and acid hydrolysis to give acid salts of I (R4 = H). Thus, acetylation of oxycodone (I; R = Me; R1R2 = O; R3 = HO; R4 = Me; Z = O) gave I (R3 = AcO), which was treated with H2C:CHO2CCl to give I (R = Me; R1R2 = O; R3 = AcO; R4 = CO2CH:CH2; Z = O) (II). Deacylation of II in CH2Cl2 containing HCl gave 14-acetylnoroxycodone hydrochloride (I.HCl; R = Me; R1R2 = O; R3 = AcO; R4 = H; Z = O) (III). III was neutralized and alkylated by cyclopropylmethyl bromide and allyl bromide to give I (R = Me; R1R2 = O; R3 = AcO; R4 = cyclopropylmethyl, allyl; Z = O).

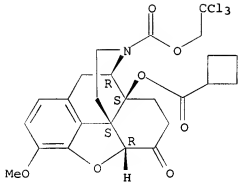
IT 70866-71-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of, demethylation by)

RN 70866-71-6 CAPLUS

CN Morphinan-6-one, 14-[(cyclopropylcarbonyl)oxy]-4,5-epoxy-3-methoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

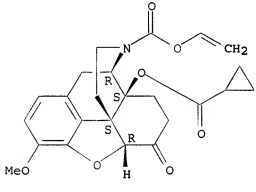
Absolute stereochemistry.





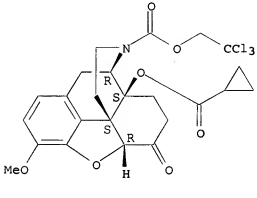
RN 70866-72-7 CAPLUS
CN Morphinan-17-carboxylic acid, 14-[(cyclopropylcarbonyl)oxy]-4,5-epoxy-3-methoxy-6-oxo-, ethenyl ester, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



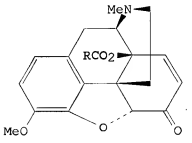
RN 70866-73-8 CAPLUS
CN Morphinan-17-carboxylic acid, 14-[(cyclopropylcarbonyl)oxy]-4,5-epoxy-3-methoxy-6-oxo-, 2,2,2-trichloroethyl ester, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

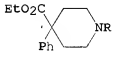


L4 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:132596 CAPLUS
DOCUMENT NUMBER: 90:132596

ORIGINAL REFERENCE NO.: 90:20871a,20874a
TITLE: QSAR of narcotic analgetic agents
AUTHOR(S): Lien, E. J.; Tong, G. L.; Srulevitch, D. B.; Dias, C.
CORPORATE SOURCE: Sect. Biomed. Chem., Univ. Southern California Sch. Pharm., Los Angeles, CA, USA
SOURCE: NIDA Research Monograph (1978), 22, 186-96
CODEN: MIDAD4; ISSN: 0361-8595
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



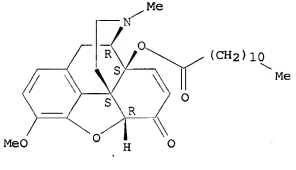
II

AB The analgesic activities of a series of 14-hydroxycodeine esters (I) was correlated with such mol. parameters as the partition coeffs. (between octanol and water), the substituent consts., and the mol. weight There appeared to be a good correlation between lipophilicity and the analgesic activity. The correlation between the analgesic activity of some meperidine homologs (II; R = alkyl), their interaction with the opiate receptor, the partition coeffs. (octanol-phosphate), and the substituent consts. was also determined

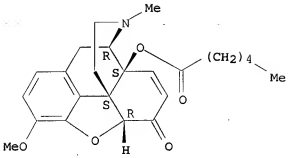
IT 51-94-5 62-58-8 748-36-7 750-54-9
751-00-8 751-01-9 909-94-4 915-25-3
1107-74-0 1250-84-6 1253-20-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesic activity of)

RN 51-94-5 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(1-oxododecyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

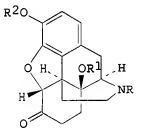
Absolute stereochemistry.



RN 62-58-8 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(1-oxoheptyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)



L4 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1977:568236 CAPLUS
DOCUMENT NUMBER: 87:168236
ORIGINAL REFERENCE NO.: 87:26599a,26602a
TITLE: An efficient synthesis of N-cyclobutylmethylnoroxymorphone from thebaine
AUTHOR(S): Olofson, R. A.; Pepe, Joseph P.
CORPORATE SOURCE: Chem. Dep., Pennsylvania State Univ., University Park, PA, USA
SOURCE: Tetrahedron Letters (1977), (18), 1575-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

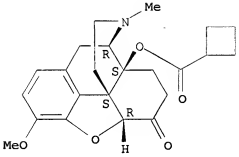
AB Protection of the 14-OH group of oxycodone (I; R = R2 = Me, R1 = H (by cyclobutylcarbonylation followed by N-demethylation with ClCO2CH:CH2 and acid hydrolysis gave I (R = H.HCl, R1 = cyclobutylcarbonyl, R2 = Me). The latter rearranged to I (R = cyclobutylcarbonyl, R1 = H, R2 = Me) on shaking with aqueous NaHCO3. Subsequent ketalization, LiAlH4 reduction, acid hydrolysis, and O-demethylation gave nalbuphine I (R = cyclobutylmethyl, R1 = R2 = H) which was obtained in 58.4% overall yield from oxycodone (49% overall yield from thebaine).

IT 64643-74-9P 64643-75-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate in noroxymorphone preparation)

RN 64643-74-9 CAPLUS

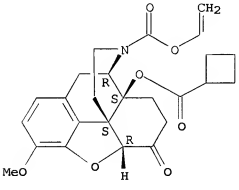
CN Morphinan-6-one, 14-[(cyclobutylcarbonyl)oxy]-4,5-epoxy-3-methoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 64643-75-0 CAPLUS
CN Morphinan-17-carboxylic acid, 14-[(cyclobutylcarbonyl)oxy]-4,5-epoxy-3-methoxy-6-oxo-, ethenyl ester, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:88183 CAPLUS
DOCUMENT NUMBER: 74:88183
ORIGINAL REFERENCE NO.: 74:14317a
TITLE: Analgesic N-substituted 14-acyloxydihydronorcodeinones
INVENTOR(S): Buckett, William R.; Bosman, Hans H.
PATENT ASSIGNEE(S): Organon Laboratories Ltd.
SOURCE: Ger. Offen., 17 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2022899	A	19701119	DE 1970-2022899	19700511
GB 1300419	A	19721220	GB 1969-25025	19690516
ZA 7003011	A	19710527	ZA 1970-3011	19700504
CH 549572	A	19740531	CH 1970-7231	19700514
NL 7007167	A	19701118	NL 1970-7167	19700515
FR 2051532	A1	19710409	FR 1970-17828	19700515
FR 2051532	A5	19710409		
SE 359093	B	19730820	SE 1970-6706	19700515
US 3828050	A	19740806	US 1972-278240	19720807
PRIORITY APPLN. INFO.:			GB 1969-25025 A	19690516
			US 1970-35881 A2	19700508

GI For diagram(s), see printed CA Issue.

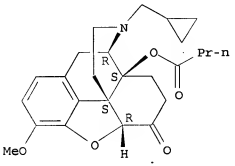
AB The analgesic, sedative, spasmolytic, antitussive title compds. (I, R = acyl) were prepared Thus, refluxing I (R = dimethylallyl, R1 = H) and Ac2O in C6H 1.5 hr gave I (R = dimethylallyl, R1 = Ac). Among about 15 compds. similarly prepared were I (R and R1 given): CH2:CHCH2, Ac; cyclobutylmethyl, Ac; dimethylallyl, EtCO; cyclopropyl-methyl, PrCO; dimethylallyl, PhCH:CHCO.

IT 30994-05-9P 30994-06-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 30994-05-9 CAPLUS

CN Morphinan-6-one, 17-(cyclopropylmethyl)-4,5α-epoxy-14-hydroxy-3-methoxy-, butyrate (ester) (8CI) (CA INDEX NAME)

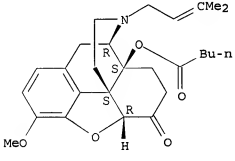
Absolute stereochemistry.



RN 30994-06-0 CAPLUS

CN Morphinan-6-one, 4,5α-epoxy-14-hydroxy-3-methoxy-17-(3-methyl-2-butenyl)-, valerate (ester) (8CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1968:103752 CAPLUS
DOCUMENT NUMBER:	68:103752
ORIGINAL REFERENCE NO.:	68:20015a,20018a
TITLE:	Physical dependence producing capacity of 14-cinnamoyloxycodeinone
AUTHOR(S):	Buckett, W. R.
CORPORATE SOURCE:	Organon Lab., Ltd., Newhouse, UK
SOURCE:	Neuro-Psycho-Pharmacol., Proc. Int. Congr. Coll. Int. Neuro-Psycho-Pharmacol., 5th (1967), Meeting Date 1966, 1243-6 CODEN: 19QBAV
DOCUMENT TYPE:	Conference
LANGUAGE:	English

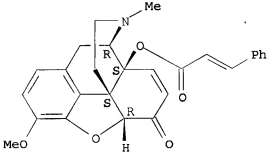
AB The phys. dependence producing capacity (PDC) of 14-cinnamoyloxycodeinone, a potent morphinelike analgesic agent, was studied in rats. Preliminary studies with the compound showed a high Straub Index in mice, low mean effective dose (0.023 mg./kg.) for analgesic effect in the rat tail pressure test, and production of the characteristic mania and rage in cats, strongly suggestive of a high PDC for 14-cinnamoyloxycodeinone. Direct demonstration of PDC was made by adding the drug to the drinking water of five rats in increasing concns. Spontaneous withdrawal or challenge with levallorphan gave severe withdrawl syndromes. Rats treated parenterally with 14-cinnamoyloxycodeinone exhibited consistant signs of dependence over long periods.

IT 751-01-9
RL: BIOL (Biological study)
(dependence on)

RN 751-01-9 CAPLUS

CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(1-oxo-3-phenyl-2-propenyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L4 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:14132 CAPLUS
DOCUMENT NUMBER: 64:14132
ORIGINAL REFERENCE NO.: 64:2626f-g
TITLE: Some pharmacological studies with 14-(cinnamoyloxy)codeinone
AUTHOR(S): Buckett, W. R.
CORPORATE SOURCE: Pharm. Inds., Ltd., Edinburgh, UK
SOURCE: Journal of Pharmacy and Pharmacology (1965), 17(11), 759-60
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: English

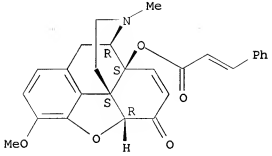
AB The pharmacol. properties of 14-(cinnamoyloxy)codeinone (I) were comparatively studied with morphine (II) in mice. There was a big difference between L.D.50 values by intravenous and by subcutaneous or oral administration for I but not for II. I was a potent analgesic, the onset and duration of analgesia in mice were shorter but more intense and depressant than the equiactive dose of II. I was shown to differ from II in its ability to produce catalepsy at a dose close to analgesic doses.

IT 751-01-9, Codeinone, 14-hydroxy-, 14-cinnamate (ester)
(analgesic activity and toxicity of, morphine and)

RN 751-01-9 CAPLUS

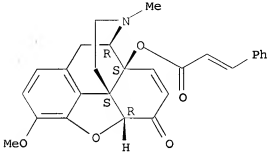
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(1-oxo-3-phenyl-2-propenyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



IT 751-01-9P, Cinnamic acid, ester with 14-hydroxycodeinone
RL: PREP (Preparation)
(preparation of)
RN 751-01-9 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(1-oxo-3-phenyl-2-propenyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

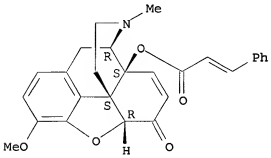
Absolute stereochemistry.
Double bond geometry unknown.



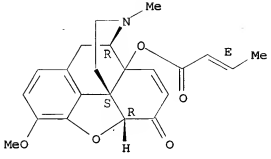
L4 ANSWER 31 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1966:14131 CAPLUS
DOCUMENT NUMBER: 64:14131
ORIGINAL REFERENCE NO.: 64:2626d-f
TITLE: Comparison of the antianaphylactic properties of ethanolamine and hydrocortisone
AUTHOR(S): Goadby, P.; Smith, W. G.
CORPORATE SOURCE: Tech. Coll., Sunderland, UK
SOURCE: Journal of Pharmacy and Pharmacology (1965), 17(11), 721-7
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antianaphylactic effects of ethanolamine (I) and hydrocortisone (II) were comparatively studied in guinea pigs. Both I and II potentiate the antianaphylactic activity of mepyramine in actively sensitized guinea pigs subjected to anaphylactic shock by exposure to aerosols of antigen solns. After intramuscular injection, the maximum effect with I occurred 1 hr. later, whereas with II it occurred 18 hrs. later. I and II were also effective after 48 min. and 12 hrs., resp., as aerosols. The optimum intramuscular dose of I was 10 mg./kg. and that of II 100 mg./kg. After aerosol administration, optimum effects were observed when 5% solns. of either I or II were used.
IT 751-01-9P, Cinnamic acid, ester with 14-hydroxycodeinone
RL: PREP (Preparation)

(preparation of)
RN 751-01-9 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(1-oxo-3-phenyl-2-propenyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

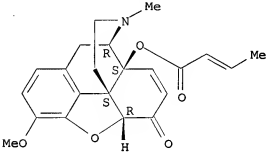


L4 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:32465 CAPLUS
DOCUMENT NUMBER: 62:32465
ORIGINAL REFERENCE NO.: 62:5773b-e
TITLE: The relation between analgesic activity, acute toxicity, and chemical structure in esters of 14-hydroxycodeinone
AUTHOR(S): Buchett W. R.
CORPORATE SOURCE: Pharm. Inds. Ltd., Edinburgh, UK
SOURCE: Journal of Pharmacy and Pharmacology (1964), 16(Suppl.), 68-71
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The L.D.50 in mice for codeinone phosphate and 14-substituted hydroxycodeinones was calculated for the intravenous and intraperitoneal routes after administration of 0.2 mg./20 g. body weight After intravenous administration, death occurred rapidly following convulsions, or catalepsy and respiratory depression. By the subcutaneous route, death occurred later. The acute toxicities decreased with a change from codeinone to 14-hydroxycodeinone and through the acetoxy to the propionoxy compound By the intravenous route, increasing the C number (from the butyrate to the hexoate) increased the toxicity. Further increase up to lauroyloxy decreased the toxicities and further increase caused death by acute respiratory depression regardless of the route of administration. The 14-phenylalkoxy derivs. were more toxic intravenously than subcutaneously. Replacing the single bond between the methylene groups in the side chain with a double bond increased the acute toxicity and changed the mode of action. Esterification of 14-hydroxycodeinone enhanced the analgesic potency of the derivs. tested on mice. Increasing the length of the acylating group increased the potency, with maximum potency being obtained with 14-heptoyloxycodeinone (60 times that of morphine hydrochloride). Further increases reduced the potency up to 14-lauroyloxycodeinone which had 1/30 the activity of morphine. The onset and duration of analgesia of these compds. were shorter than for either codeine or morphine.
IT 748-36-7
(Derived from data in the 7th Collective Formula Index (1962-1966))
RN 748-36-7 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(1-oxo-2-butenyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)



L4 ANSWER 33 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:32464 CAPLUS
DOCUMENT NUMBER: 62:32464
ORIGINAL REFERENCE NO.: 62:5773a-b
TITLE: Hypoglycemic properties of tecomine and tecostanine
AUTHOR(S): Hammouda, Youssef; Rashid, Abdel Kadar; Amer, M. Samir
CORPORATE SOURCE: Fac. Pharm., Alexandria, Egypt
SOURCE: Journal of Pharmacy and Pharmacology (1964), 16(12), 833-4
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The biol. assay for hypoglycemic properties of 2 alkaloids compared with tolbutamide was described. Normal healthy albino rabbits weighing 1.5-2 kg. fasted for 12 hrs. were injected with tecomine and tecostanine salt solns. in isotonic saline. Tecomine and tecostanine were potent hypoglycemic agents when given intravenously. The average lethal dose was 300 mg./kg. in mice.
IT 748-36-7
(Derived from data in the 7th Collective Formula Index (1962-1966))
RN 748-36-7 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(1-oxo-2-butenyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L4 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:406898 CAPLUS
DOCUMENT NUMBER: 61:6898
ORIGINAL REFERENCE NO.: 61:1119f-g
TITLE: Analgesic properties of some 14-substituted derivatives of codeine and codeinone
AUTHOR(S): Buckett, W. R.; Farquharson, Muriel E.; Haining, C. G.

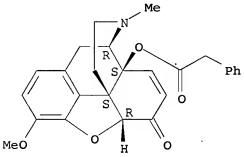
CORPORATE SOURCE: Edinburgh Pharm. Ind. Ltd., UK
SOURCE: Journal of Pharmacy and Pharmacology (1964), 16, 174-62
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The effects of 14-hydroxylation and subsequent 14-acylation on the toxicity and analgesic activity of codeine, codeine 6-acetate, codeinone, and Δ7 deoxycodeine were examined in rats and mice. Acute toxicity was reduced in each instance by the introduction of a 14-hydroxy group and was not generally enhanced by its esterification. 14 Acetoxycodeine was approx. equal to morphine in potency and esterification at the 14-position of hydroxycodeine with other straight-chain aliphatic acids containing up to 5 C atoms failed to enhance potency further. 14-Benzolation of either 14-hydroxycodeine or 14-hydroxycodeinone had little effect on analgesic activity but the introduction of a methylene group between the carboxyl group and the phenyl ring enhanced potency considerably in each case. Increasing the number of C atoms from 2 to 5 in the 14-acyl groups of esters of 14-hydroxycodeinone and 14 hydroxy-Δ7-deoxycodeine led to a gradual increase in analgesic activity. In rats the n-valeryl ester of 14-hydroxy-Δ7-deoxycodeine was estimated to have 75 times the potency of morphine.

IT 750-54-9, Codeinone, 14-hydroxy-, phenylacetate(ester)
909-94-4, Codeinone, 14-hydroxy-, butyrate (ester)
1250-84-6, Codeinone, 14-hydroxy-, valerate (ester)
104134-14-7, Codeinone, 14-hydroxy-, nicotinate(ester)
900789-20-0, Nicotinic acid, ester with 14-hydroxycodeinone
900789-24-4, Nicotinic acid, ester with 14-hydroxycodeine, hydrochloride
(analgesic activity of)

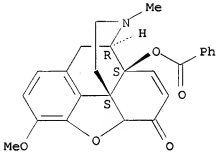
RN 750-54-9 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(phenylacetyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



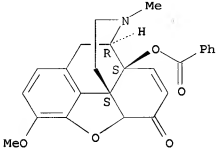
RN 909-94-4 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-(1-oxobutoxy)-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 900789-24-4 CAPLUS
CN Nicotinic acid, ester with 14-hydroxycodeine, hydrochloride (7CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L4 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1964:9952 CAPLUS
DOCUMENT NUMBER: 60:9952
ORIGINAL REFERENCE NO.: 60:1816a-c
TITLE: Dihydrohydroxycodeinone nicotinic acid ester
INVENTOR(S): Pongratz, Alfred; Zirm, Konrad L.
PATENT ASSIGNEE(S): Lannacher Heilmittel G.m.b.H.
SOURCE: 2 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AT 229496		19630925	AT	19610308
PRIORITY APPLN. INFO.:			AT	19610308

AB The nicotinic acid ester I of dihydrohydroxycodeinone (II) and salts thereof are prepared by treating II, preferably as the free base, with nicotinic acid anhydride (III) in the presence of solvents, e.g., pyridine or other tertiary bases, aromatic, aliphatic, or hydroaromatic hydrocarbons, halogenated aliphatic hydrocarbons, or mixts. thereof. The reaction is preferably conducted at the b.p. of the solvent used. Thus, 5 parts by weight II is refluxed 8 hrs. with 8 III in a mixture of 10 volume parts

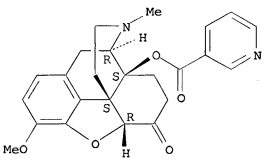
C6H6 and 5 of a petroleum fraction b. 50-80°, the solvent is evaporated, the residue taken up in 50 volume parts H2O, NaHCO3 added until no more CO2 is formed, the pH is adjusted to 9, and I, m. 235-6.5°, allowed to crystalline; it is useful as an analgesic.

IT 103131-86-8
(Derived from data in the 7th Collective Formula Index (1962-1966))

RN 103131-86-8 CAPLUS

CN Morphinan-6-one, 4,5-epoxy-3-methoxy-17-methyl-14-[(3-pyridinylcarbonyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1964:9951 CAPLUS

DOCUMENT NUMBER: 60:9951

ORIGINAL REFERENCE NO.: 60:1812e-h,1813a-h,1814a-h,1815a-e,1816a

TITLE: Structure of the 2-acylindole alkaloids vobasine, dregamine, and tabernaemontanine

AUTHOR(S): Renner, U.; Prins, D. A.; Burlingame, A. L.; Biemann, K.

CORPORATE SOURCE: J. R. Geigy A.-G., Basel, Switz.

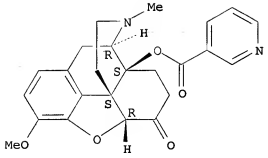
SOURCE: Helvetica Chimica Acta (1963), 46(6), 2186-208
CODEN: HCACAV; ISSN: 0018-019X

DOCUMENT TYPE: Journal

LANGUAGE: German

GI For diagram(s), see printed CA Issue.

AB cf. CA 59, 7625b; CA 56, 8778e. Ground trunk bark (30 kg.) of Voacanga africana was stirred at room temperature with two 100-l. vols. MeOH, the extract centrifuged, concentrated in vacuo to about 10-l., treated with 50 1.2N AcOH, and residual MeOH distilled in vacuo. The acid solution was clarified by suction filtration through diatomaceous earth, pH adjusted to 3.3, and stirred with five 10-l. vols. C6H6. he extracted aqueous solution was cooled, stirred, and made alkaline with concentrated NH3, the precipitated crude bases (1.5 kg.) filtered off with suction, washed with H2O, dried, and extracted with C6H6, which extract was evaporated in vacuo to give 750 g. C6H6-soluble total alkaloids. A 170-g. portion of this material was chromatographed on 6 kg. neutral Al2O3 (activity II, Brockmann). Elution with C6H6 and C6H6-Et2O (9:1) gave 65.5 g. of a mixture of voacangine, voacamine, and vobtusine. Further elution with C6H6-Et2O (9:1 and 1:1) gave 83.5 g. mixture yielding 25.5 g. voacorine on crystallization from MeOH. The mother liquor was evaporated to dryness in vacuo and the residue (50 g.) dissolved in 250 ml. 2N AcOH, diluted with 500 ml. H2O, stirred, and treated with about 1.5 l. saturated aqueous KBr at room temperature The precipitated hydrobromide was filtered off with suction, the filtrate treated



L4 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1963:415846 CAPLUS
DOCUMENT NUMBER:	59:15846
ORIGINAL REFERENCE NO.:	59:2885f-h
TITLE:	14-Acyloxycodeinones
INVENTOR(S):	Spring, Frank S.; Haining, Colin G.; Newbold, Geoffrey T.
PATENT ASSIGNEE(S):	T. & H. Smith Ltd.
SOURCE:	2 pp.
DOCUMENT TYPE:	Patent
LANGUAGE:	Unavailable
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 919313		19630220	GB 1961-82661	19581028
PRIORITY APPLN. INFO.:			GB	19581028

GI For diagram(s), see printed CA Issue.

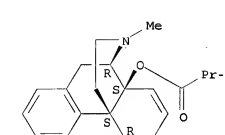
AB The title compds. were prepared by the direct acylation of 14-hydroxycodeinone (I). Thus, 2.0 g. I was heated with 10 cc. (PrCO)2O on a steam bath with occasional shaking, the solution was then warmed with H2O to destroy excess (PrCO)2O, cooled with ice, and basified with 0.880N NH4OH to provide a crude product, which was crystallized from C6H6-petr. ether to give 1.7 g. 14-propionoxycodeinone, m. 182-3°, [α]17D -91° (c 1.3, CHCl3). Similarly prepared were: 14-butyryloxyeodeinone, m. 152.0-3.5°, [α]17D -89° (c 2.0, CHCl3); 14-valeryloxycodeinone (II), m. 133-4°, [α]17D -80° (c 3.6, CHCl3). II was also prepared by acylating I with BuCOCl, m. 133-4°, [α]17D -77° (c 1.0, CHCl8).

IT 909-94-4P, Codeinone, 14-hydroxy-, butyrate (ester)
1250-84-6P, Codeinone, 14-hydroxy-, valerate (ester)
RL: PREP (Preparation)
(preparation of)

RN 909-94-4 CAPLUS

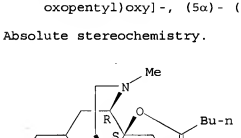
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-(1-oxobutoxy)-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 1250-84-6 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(1-oxopentyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1962:60718 CAPLUS
DOCUMENT NUMBER: 56:60718
ORIGINAL REFERENCE NO.: 56:11638b-i,11639a-h
TITLE: 14-Hydroxynorcodeine and its derivatives
AUTHOR(S): Currie, A.C.; Newbold, G. T.; Spring, F. S.
CORPORATE SOURCE: Roy. Coll. Sci. Technol., Glasgow, UK
SOURCE: Journal of the Chemical Society (1961) 4693-700
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Reduction of 14-acyloxy-N-cyanonoreodeine derivs. by LiAlH4 gave 14-hydroxynorcodeine (I). N-Acyl derivs. of the latter were prepared from the corresponding 14-acyloxy-N-cyano compound by acyl migration. Reduction of the N-acyl compds. with LiAlH4 gave the N-alkyl-14-hydroxynorcodeines. 14-Acetoxycodeine acetate (6 g.) heated 3 min. at 100° with 10 g. CNBr gave 5 g. 14-acetoxy-N-cyanonorcodeine 6-acetate (II), prisms, m. 190°, [α]D -123° (c 0.8). 14-Acetoxycodeinone (III) (4 g.) heated 6 min. at 100° with 8 g. CNBr gave 3.5 g. 14-acetoxy-N-cyanonorcodeinone (IV), m. 260-2°, [α]D -60° (c 1.9). III (5 g.) in 400 cc. CHCl3 refluxed 2 hrs. with 20 g. CNBr gave 4 g. IV. IV (1 g.) in 75 cc. dioxane stirred 2 hrs. with 0.5 g. NaBH4 in 10 cc. H2O, extracted with CHCl3, and crystallized gave 0.8 g. 14 acetoxy-N-cyanonorcodeine (V), prisms, m. 220-2°, [α]D -69° (c 0.9). II (2 g.) reduced with NaBH4 gave 1.8 g. unchanged II and 0.1 g. V. II (0.2 g.) in 75 ml. MeOH refluxed 5 hrs. with 4 cc. pyridine gave 0.15 g. V. V gave its 6-acetate and with MnO2 IV. 14-Acetoxydihydronorcodeinone (10 g.) in 500 cc. CHCl3 refluxed with 30 g. CNBr in 200 cc. CHCl3 gave 14-acetoxy-N-cyanodihydronorcodeinone (VI),

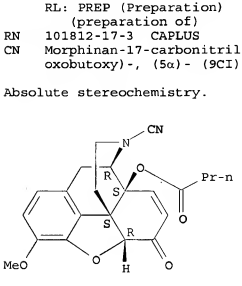
dioxane stirred 2 hrs. with 200 mg. NaBH4 in 5 cc. H2O and the gum heated 3 hrs. with 5 cc. propionic anhydride gave XVI. VIa (400 mg.) similarly reduced to a gum, then refluxed 12 hrs. with 250 mg. KOH in 25 cc. MeOH and 0.5 cc. H2O, and the 230 mg. solid product heated 3 hrs. with 5 cc. propionic anhydride gave 130 mg. XVI. 14-Butyryloxy-N-cyanonorcodeinone (0.6 g.) in 35 cc. PrCO2H and 15 cc. H2O refluxed 18 hrs. gave 0.6 g. Nbutyryl-14-hydroxynorcodeinone (XVII), amorphous, m. 185-90°, [α]D -162° (c 0.2). 14-Butyryloxy-N-cyanonorcodeinone (3 g.) in 100 cc. dioxane stirred 2 hrs. with 1.5 g. NaBH4 in 20 cc. H2O, the gum refluxed 18 hrs. with 1 g. KOH in 100 cc. MeOH and 1 cc. H2O, extracted with CHCl3, and the 1.8 g. treated 1 hr. with 4.5 g. active MnO2 gave 1.5 g. XVII. VIII (100 mg.) suspended in 200 cc. Et2O cooled and treated with 250 mg. LiAlH4 in 20 cc. Et2O, refluxed 2 hrs., decomposed, and the product crystallized gave 90 mg. N-ethyl-14-hydroxynorcodeine (XVIII), prisms, m. 128°, [α]D -105° (c 0.3). XII and its acetate were similarly reduced to yield XVIII. N-Ethyl-14-hydroxynorcodeine (60 mg.) in 5 cc. CHCl3 stirred 1 hr. with MnO2 gave 50 mg. N-ethyl-14-hydroxynorcodeinone (XIX), prisms, m. 230° (decomposition), [α]D -220° (c 1.0). XIX (100 mg.) in 25 ml. dioxane treated with 100 mg. NaBH4 in 3 cc. H2O, after 2 hrs. 500 cc. H2O added, solid extracted with CHCl3, and the gum crystallized gave 100 mg. XVIII. XVIII with Ac2O gave the acetate, prisms, m. 183-5°, [α]D -115° (c 0.2). XVIII with Ac2O 1 hr. at 100° gave 14-acetoxy-N-ethylnorcodeine (XX), m. 224-5°, [α]D -83° (c 0.3). 14-Acetoxy-N-ethylnorcodeinone (350 mg.) in 20 cc. dioxane reduced with 200 mg. NaBH4 in 5 cc. H2O gave XX. XVIII (100 mg.) in 10 cc. Ac2O refluxed 1 hr. gave 80 mg. 14-acetoxy-N-ethylnorcodeine 6-acetate (XXI), prisms, m. 170-1°, [α]D -143° (c 0.4). XXI (100 mg.) heated 3 min. at 100° with 1 g. CNBr gave II. XVI (400 mg.) in 10 cc. tetrahydrofuran and 90 cc. Et2O refluxed 4 hrs. after the addition of 300 mg. LiAlH4 gave 300 mg. 14-hydroxy-N-propylnorcodeine (XXII), prisms, m. 111-12°, [α]D -121° (c 1.5). XXII (100 mg.) in 5 cc. CHCl3 stirred 1 hr. with 500 mg. MnO2 gave 100 mg. 14-hydroxy-N-propylnorcodeinone, m. 126-7°, [α]D -208° (c 0.6); 14-acetate, m. 178°, [α]D -102° (c 1.1).

IT 101812-17-3P, Norcodeinone, N-cyano-14-hydroxy-, 14-butyrate
RL: PREP (Preparation)
(preparation of)

RN 101812-17-3 CAPLUS

CN Morphinan-17-carbonitrile, 7,8-didehydro-4,5-epoxy-3-methoxy-14-(1-oxobutoxy)-, (5α)- (9CI) (CA INDEX NAME)

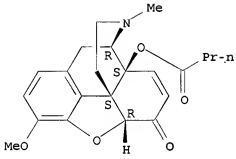
Absolute stereochemistry.



L4 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1960:74784 CAPLUS
DOCUMENT NUMBER: 54:74784
ORIGINAL REFERENCE NO.: 54:14291a-i,14292a-d
TITLE: Some reactions of 14-hydroxycodeine

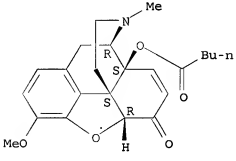
AUTHOR(S): Currie, A. C.; Gillon, John; Newbold, G. T.; Spring, F. S.
CORPORATE SOURCE: Roy. Coll. Sci. & Technol., Glasgow, UK
SOURCE: Journal of the Chemical Society (1960) 773-81
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB 14-Hydroxycodeine (I) was prepared by treating 10 g. 14-hydroxycodeinone (II) with 10 g. LiAlH4 (III) in 350 ml. boiling ether. Treating the mixture with ice, washing with water, and evaporating gave 9.15 g. gum, which crystallized from benzene-petr. ether to yield 8.0 g. I, m. 155-7°, [α]D -129.5° (c 1.75) (all rotations measured in chloroform). II (1.0 g.) in 25 ml. boiling dioxane was cooled to 15°, treated with 1.2 g. NaBH4 (IV) in 10 ml. water, stirred 2 hrs., after dilution with 100 ml. 2N NaOH I extracted with CHCl3, and crystallized as above. I hydrochloride, m. 263-4°, was obtained by treating a CHCl3 solution of I with dry HCl. II (4 g.) was treated with 5 g. (iso-PrO)3Al in 50 ml. dry iso-PrOH until all the acetone was removed. I (2.75 g., 69%) was obtained by removing the excess alc., treating with water and NH3, and extracting with CHCl3. I was treated with Ac2O on a steam bath 1.5 hrs. Crystallization yielded 14-acetoxycodeine 6-acetate (V), m. 198-200°, [α]D -126° (c 1.5). The hydrochloride, m. 164-7° (decomposition), was prepared V (5 g.) in 100 ml. MeOH was refluxed 4 hrs. and concentrated to give unreacted V. Further concentration and recrystn. yielded 1.5 g. 14-hydroxycodeine 6-acetate (VI), m. 155-6°, [α]D -220° (c 6.0). Acetylation of VI gave V. II (2.0 g.) with 10 ml. (EtCO)2O gave 1.7 g. 14-propionyloxycodeinone, m. 182-3°, [α]D -91° (C 1.3). Similarly, (PrCO)2O yielded 14-butyryloxycodeinone, m. 152.5-3.5°, [α]D -87° (c 2.0). 14-Valeryloxycodeinone, m. 133-4°, [α]D -77° (c 1.0), was prepared from the acid chloride and pyridine and from the acid anhydride. The appropriate 14-acyloxycodeinones with IV gave the following 14-acyloxycodeines [acyl, m.p., [α]D (c), m.p. (decomposition) of HCl salt given]: AcO (VI), 203-5°, -64° (1.2) [-61° (1.0)], 222-4°; EtCO (VII), 164-5.5°, -54° (1.0, 1.7), 165-70°; PrCO, 131-2°, -49° (1.0), 165°; BuCO, 110-11°, -47° (1.4), 138-48°; Bz (VIII), 221-2°, -120° (1.2) [-124° (1.0)], 177-80°. Acetylation of VII and VIII gave VII 6-acetate, m. 153-4°, [α]D -127°, -129° (c 1.7, 1.3) [HCl salt m. 215-20° (decomposition)], and VIII 6-acetate, m. 194-5°, [α]D -174°, -168° (c 2.0, 6.0); HCl salt m. 227-9° (decomposition). Hydrogenation of I in AcOH and H2O gave dihydro-14-hydroxycodeine (IX), m. 140-1°, [α]D 169° (c 0.6), acetylated to the diacetate, m. 180.5-1.5°, [α]D -211° (c 1.3). Hydrogenation of VI gave 14-acetoxydihydrocodeine (X), m. 164-6°, [α]D -202° (c 1.6). X.HCl, m. 175-82° (decomposition), was prepared Hydrogenation of V gave 14-acetoxydihydrocodeine 6-acetate, m. 181.5-2.5°, [α]D -206° (c 1.0). Dihydro-14-hydroxycodeinone (XI) (5.0 g.) was reduced with 3 g. IV to the less soluble dihydro-14-hydroxyisocodeine (XII), m. 167-8°, [α]D -142° (c 1.3). Acetylation of XII gave the diacetate (XIII), m. 199-201°, [α]D -198° (c 1.4). XIII.HCl, m. 197-201° (decomposition), was prepared IX was also obtained from the reduction of XI. 14-Acetoxydihydrocodeinone was reduced with IV. After 6 recrystns. from benzene-petr. ether, 14-acetoxydihydroisocodeine (XIV), m. 180-2°, [α]D -177° (c 1.3), was obtained. XIII was prepared from XIV. II was prepared by treating I with MnO2 in CHCl3 at room temperature IX is oxidized with tert-BuOK and Ph2CO to dihydro-14-hydroxycodeinone, m. 218-19°, [α]D -217° (c 1.3). Oxidation of XII gave XI. I (5 g.) in 10



RN 1250-84-6 CAPLUS
CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(1-oxopentyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1960:74783 CAPLUS
DOCUMENT NUMBER: 54:74783
ORIGINAL REFERENCE NO.: 54:14290e-i,14291a
TITLE: Alkaloids from Aspidosperma australe. II. Structure of olivacine and U-alkaloid C (guatambuine)
AUTHOR(S): Ondetti, Miguel A.; Deulofeu, Venancio
CORPORATE SOURCE: E. R. Squibb & Sons, Argentina S. A., Buenos Aires
SOURCE: Tetrahedron Letters (1960), (No. 1), 18-22
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. CA 53, 22727h. Degradation of olivacine (I) gave products identical with those from uleine (II) (Bchi and Warnhoff, CA 54, 6773i). Hofmann degradation of the MeI salt (II) of N-methyltetrahydroolivacine (III) gave an unsatd. tertiary base (IV) and a 2nd base (V) unchanged by hydrogenation. IV was converted into a new crystalline MeI salt (VI), C20H25IN2, m. 284-5°, δ 241, 280 mμ, showing characteristic H2C:CH bands in the IR spectrum. IV hydrogenated with PtO2 and the product treated with MeI gave a saturated MeI salt (VII), m. 287-8°, δ 240, 250, 262, 298 mμ, with an IR spectrum identical with that of a MeI salt, m. 295-6°, prepared from II MeI salt by Hofmann degradation Hofmann degradation of VII produced a new methine, m. 65-7°, δ 258, 299 mμ, with IR spectrum superimposable on that of the methine obtained from the similar MeI salt prepared from II. Hydrogenation of the methine produced a compound, m. 74.5-5.5°, δ 240, 248, 261, 298 mμ, with IR spectrum identical with that of the compound, m. 76.5-7.0, obtained from II by a double Hofmann degradation and hydrogenation. Accordingly, III

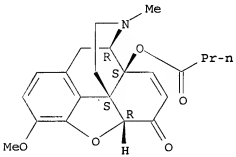
[(+)-guatambuine (CA 53, 22749i)] has the assigned structure which is in agreement with the formation of an optically inactive methine by Hofmann degradation of guatambuine methiodide, identical with that obtained from II. V yielded a MeI salt, m. 262-3°, δ 240, 250, 261, 297 mμ, IR spectrum differing from those recorded for VI and VII.

IT 909-94-4 1250-84-6
(Derived from data in the 6th Collective Formula Index (1957-1961))

RN 909-94-4 CAPLUS

CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-(1-oxobutoxy)-, (5α)- (9CI) (CA INDEX NAME)

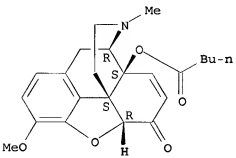
Absolute stereochemistry.



RN 1250-84-6 CAPLUS

CN Morphinan-6-one, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-14-[(1-oxopentyl)oxy]-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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FILE 'REGISTRY' ENTERED AT 11:01:09 ON 03 DEC 2007
L1 STRUCTURE UPLOADED
L2 11 S L1
L3 261 S L1 FULL

FILE 'CAPLUS' ENTERED AT 11:01:39 ON 03 DEC 2007
L4 40 S L3

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L1 HAS NO ANSWERS
L1 STR

10/519,388

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

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